UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader
January 15, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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AND TOXIC SUBSTANCES

January 13, 1999

MEMORANDUM

SUBJECT: **METHIDATHION**. Revised Short Format HED Chapter of RED. Chemical Number 100301. DP Barcode D252049.

FROM: Robert Travaglini, Chemist
Risk Characterization and Analysis Branch
Health Effects Division (7509)C

THROUGH: Steven A. Knizner, Branch Senior Scientist
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

TO: Kathy Monk, Branch Chief
Reregistration Branch 2
Special Review and Reregistration Division (7508W)

Please find enclosed a revised preliminary risk assessment for methidathion, which serves as the short (streamlined) format of the HED RED chapter for Methidathion.

This represents a revision of the October 30, 1998 Short Format HED Chapter of the RED, in response to comments received during the 30-day error correction period. Cumulative risk assessment considering risk from other pesticides which have a common mechanism of toxicity is not addressed in this document.

REVISED PRELIMINARY RISK ASSESSMENT

METHIDATHION

January 13, 1999

Risk Characterization and Analysis Branch
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

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Executive Summary

Methidathion (*O,O*-dimethyl phosphorodithioate, *S*-ester with 4-(mercaptomethyl-2-methoxy-1,3,4-thiadiazolin-5-one) is a non-systemic, organophosphate insecticide registered for control of a broad spectrum of agricultural insect and mite pests on various terrestrial food crops. Use sites include citrus, stone and pome fruits, nuts, artichokes, olives safflower, sunflower, alfalfa (grown for seed only) and cotton. Methidathion is also used on terrestrial non-food crops such as tobacco and ornamental plants (nursery stock only). Nuts, stone fruits and citrus are the predominant uses. Novartis, Inc. in agreement with Gowan Company maintains the registrations of the manufacturing use products; technical grade, 95% active ingredient (AI) and formulated intermediate (FI), 50% AI, as well the end-use product: 25% AI wettable powder (WP) which are restricted use pesticides. The registrants also maintain registrations of two emulsifiable concentrate products (ECs) which are not marketed or produced at this time. Application rates for methidathion range from 0.25 to 10 lb ai/acre.

The toxicology database is complete and provides overwhelming evidence confirming that methidathion, like other organophosphates, has anticholinesterase activity in all species tested, including dogs, rabbits, rats, and hens. By the oral route, technical methidathion is classified in Toxicity Category I. By dermal routes, technical methidathion is placed in Toxicity Category II and by the inhalation route in Toxicity Category III. Methidathion is a mild eye irritant (Toxicity Category III), is not a skin irritant (Toxicity Category IV) and is not a dermal sensitizer. Methidathion did not induce organophosphate induced delayed neuropathy (OPDIN) in the hen. Following a single oral dose to rats, methidathion was associated with neurotoxicity in both sexes as evidenced by decreases in maze activity and alterations in functional observation parameters at the highest dose tested. In addition, there were statistically significant decreases in plasma, red blood cell and brain cholinesterase activity at all dose levels.

In a subchronic neurotoxicity study in rats, methidathion caused significant decreases in red blood cell, plasma and brain cholinesterase activity. Following repeated dermal applications to rabbits, males exhibited decreases in plasma, red blood cell and brain cholinesterase activity while females showed decreases only in red blood cell and brain cholinesterase activity. Chronic exposure to dogs resulted in inhibition of red blood cell and brain cholinesterase activity as well as elevation of hepatic enzymes, gross hepatic lesions and microscopic presence of bile plugs, distended bile canaliculi and chronic hepatitis.

No evidence of carcinogenicity was seen in male or female rats; however, there was evidence of carcinogenicity in male mice (benign and malignant liver tumors were seen). Methidathion is classified as a Group C, possible human carcinogen. The evidence as a whole (i.e., one sex, one species, common tumor type, no increase in proportion of malignant tumors, or apparent shortening of time to tumor, lack of mutagenicity) was not considered strong enough to warrant a quantitative estimation of human risk. In addition methidathion was non mutagenic

both *in vivo* and *in vitro*.

There was no evidence of increased susceptibility following *in utero* exposures to rats and rabbits as well as pre/post natal exposure to rats. Additionally, there was no evidence of abnormalities in the development of the fetal nervous system in these studies.

Inhibition of cholinesterase activity was the toxicity endpoint selected for acute and chronic dietary risk assessments. An Uncertainty Factor (UF) of 100 was applied to the dose selected to account for inter-species variation (10x) and intra-species extrapolation (10x). The FQPA Safety Factor Committee recommended that the 10x additional factor for the protection of infants and children should be removed because: 1) the toxicology data base is complete; 2) there was no evidence of increased susceptibility seen following *in utero* exposure to rats and rabbits; 3) there was no evidence of increased susceptibility in the offsprings in the two-generation reproduction study in rats, and 4) adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary exposure and to provide a screening level drinking water exposure assessment.

The existing residue and product chemistry database for methidathion has been reviewed and is sufficient to assess dietary exposure for the purposes of reregistration. Tolerances have been reassessed and current consumption data have been incorporated in the evaluation of the dietary exposure and assessment.

There are no registered uses of methidathion at the present time that could result in residential exposures, therefore an aggregate exposure risk assessment for methidathion includes exposure from dietary (food + water) sources only.

The acute dietary risk assessment based on statistical exposure analysis (Monte Carlo) indicate that methidathion residues in the diet does not exceed HED's level of concern for acute exposure for any of the population subgroups examined. The highly refined assessment, based on an acute reference dose of 0.002 mg/kg, and conducted at the 99.9th percentile exposure, revealed that the percentages of the RfD occupied ranged from 22% for Females (13+, nursing) to 63% for children (1-6 years).

The chronic dietary risk assessment conducted was partially refined, using some percent crop treated data and some anticipated residues. The percent of the chronic RfD occupied from dietary exposure to residues of methidathion ranged from 3% for females (13+, nursing) to 23% children (1-6 years). This assessment was based on a chronic RfD of 0.0015 mg/kg/day. The chronic dietary exposure to methidathion from its pesticidal use does not exceed HED's level of concern.

The potential dietary exposure to methidathion residues in drinking water was assessed using models for ground and surface waters. Since dietary risk assessments based on exposures solely from food do not exceed levels of concern, drinking water levels of comparison (DWLOCs) were calculated and compared to EFED water model estimates (PRIZM-EXAMS, SCI-GROW) and monitoring results. These DWLOCs do not indicate a risk concern from potential exposure to methidathion residues in drinking water.

An occupational exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers during use or to persons entering treated sites after application is complete. EPA has determined that there are potential exposures to mixers, loaders, applicators, or other handlers during usual use-patterns associated with methidathion. Based on the use patterns, eight major exposure scenarios were identified for methidathion.

Inhibition of cholinesterase activity was also the toxicity endpoint chosen for occupational risk assessments. Occupational exposure estimates to mixer, loaders and applicators were based on PHED Version 1.1 surrogate data. For the short-term and intermediate term risk assessments, a NOAEL of 0.2 mg/kg/day based on serum and brain cholinesterase inhibition was used for risk assessment. Based on these assessments, EPA feels there is serious concern for occupational exposure to methidathion via dermal and inhalation routes.

Despite the potential for post-application occupational exposure, HED has decided not to assess this exposure at this time. The decision was based on the fact that all of the short-term and intermediate-term handler MOEs were unacceptable. Until the issues surrounding the handling of methidathion can be resolved, HED decided to postpone addressing the post- application exposure.

I. Hazard assessment

A. Toxicology Assessment

The toxicity profile of methidathion is presented below in Table 1.

Table 1. Toxicity Profile of Methidathion

Study Type	MRID No.	Results	Toxicity Category
Acute Oral - Rat	00139328	LD_{50} = 46.1 mg/kg	I
Acute Dermal - Rat	00139326	LD_{50} = 1663 mg/kg	II
Acute Inhalation -Rat	00011449	LC_{50} = 19 mg/L/1hr	III
Primary Eye Irritation	00159199	Mild irritant	III
Primary Skin Irritation	00159200	Non-irritant	IV
Dermal Sensitization	00252433	Non-sensitizing	NA
Acute Delayed Neurotoxicity - Hen	00011704	NOAEL = 350 mg/kg Negative for OPIDN	NA
Acute Neurotoxicity - Rat	43145903 43590304	Cholinesterase inhibition NOAEL = < 1 mg/kg (LDT) No neuropathology	NA

Study Type	MRID No.	Results
21-Day Dermal Toxicity-Rabbit	40079804	Systemic toxicity NOAEL= 5 mg/kg/day LOAEL =20 mg/kg/day (decrease in body weight gain and hypoactivity).
21-Day Dermal Toxicity-Rabbit	40079806	Systemic toxicity NOAEL = 1 mg/kg/day (LDT) (mortality and cholinergic signs) NOAEL (ChE inhibition) = 1 mg/kg/day LOAEL (ChE inhibition) = 10 mg/kg/day
90-Day Neurotoxicity - Rat	43582501	NOAEL = 0.2 mg/kg/day LOAEL = 0.6 mg/kg/day (serum, central nervous system and red blood cell cholinesterase inhibition)
Chronic-Feeding-Dog	41945001	NOAEL = 0.15 mg/kg/day LOAEL = 1.33 mg/kg/day (hepato toxicity)
Chronic toxicity/ Carcinogenicity-Rat	00160260	NOAEL = 0.2 mg/kg/day LOAEL = 2.0mg/kg/day (brain cholinesterase inhibition) **No evidence of carcinogenicity**
Carcinogenicity-Mouse	00157457	NOAEL = 1.5 mg/kg/day LOAEL = 7.5 mg/kg/day (hepatotoxicity) **Evidence of carcinogenicity (liver tumors) only at the high dose (16.1 mg/kg/day)**
Developmental Toxicity-Rat	40079808	Maternal toxicity NOAEL = 1.0 mg/kg/day LOAEL = 2.25 mg/kg/day (decreased body weight and cholinergic clinical signs) Developmental toxicity NOAEL = $\geq$ 2.25 mg/kg/day
Developmental Toxicity-Rabbit	40079810	Maternal toxicity NOAEL = 6.0 mg/kg/day LOAEL = 12.0 mg/kg/day (cholinergic clinical signs) Developmental toxicity NOAEL= $\geq$ 12 mg/kg/day
Reproductive Toxicity	40079812 40079813	Parental/Systemic NOAEL = 0.25 mg/kg/day LOAEL = 1.25 mg/kg/day (tremors, decreased food consumption and ovarian weights) Offspring NOAEL= 0.2 mg/kg/day LOAEL = 12.5 mg/kg/day (based on decreased pup weight and an increased incidence of hypothermia with the appearance of starvation.
Gene Mutation - *Salmonella*	00078329 00078330 00084010	Non-mutagenic (±) activation.
In vivo Mouse Lymphoma	00070213 0078332	Negative
In vivo Sister Chromatid Exchange	00078335	Negative

Study Type	MRID No.	Results
In vitro (CHO bone marrow cells)	00078334	Negative
Metabolism-Rat	40127818	Methidathion was metabolized and excreted within 24 hours; urine was the primary route of elimination.

B. Dose Response Assessment

1. Determination of Susceptibility

The Hazard Identification Assessment Review Committee (HIARC)[1] evaluated the toxicology data base and concluded that there was no increased susceptibility in rat or rabbit fetuses following *in utero* exposure since no developmental toxicity was seen at the highest dose tested in either species, or in the offspring, as compared to parental animals in the two-generation reproduction toxicity study. The HIARC did not recommended a developmental neurotoxicity study in rats due to lack of evidence of (OPIDN) in the hen or neuropathology in any of the studies.

The FQPA Safety Factor Committee[2] recommended that the 10x additional factor for the protection of infants and children should be removed for the following four reasons: 1) the toxicology data base is complete; 2) there was no evidence of increased susceptibility seen following *in utero* exposure to rats and rabbits; 3) there was no evidence of increased susceptibility in the offsprings in the two-generation reproduction study in rats, and 4) adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary exposure and to provide a screening level drinking water exposure assessment.

2. Toxicology Endpoint Selection

The toxicology endpoints selected for dietary and non-dietary risk assessments are presented in Table 2.

Table 2. Toxicology Endpoints Selected for Risk Assessments

Exposure Duration	Exposure Route	Dose	Endpoint	Comments
Acute	Dietary	Acute RfD= 0.002 mg/kg	Serum and brain cholinesterase inhibition	NOAEL=0.2 mg/kg/day and an Uncertainty Factor of 100 (10x for inter-species extrapolation and 10x for intra-species variability) No FQPA Safety Factor. (90 day rat neurotoxicity study)
Chronic	Dietary	Chronic RfD= 0.0015 mg/kg/day	Erythrocyte cholinesterase inhibition	NOAEL=0.15 mg/kg/day and an Uncertainty Factor of 100 (10x for inter-species extrapolation and 10x for intra-species variability) No FQPA Safety Factor. Chronic dog feeding study

Exposure Duration	Exposure Route	Dose	Endpoint	Comments
Short-Term (1-7 Days)	Dermal [a] & Inhalation [b]	Oral NOAEL=0. 2 mg/kg/day	Serum and brain cholinesterase inhibition	A MOE of 100 is adequate for occupational exposure risk assessments. NOAEL of 0.2 mg/kg/day (from 90 day rat neurotoxicity study). **There are no uses which result in residential exposures.**
Intermediate-Term (7-90 days)	Dermal [a] & Inhalation [b]	Oral NOAEL=0. 2 mg/kg/day	Serum and brain cholinesterase inhibition	A MOE of 100 is adequate for occupational exposure risk assessments. **There are no uses which result in residential exposures.**
Long-Term (90-day to life-time)	Dermal [a] & Inhalation [b]	Oral NOAEL=0. 15 mg/kg/day	Erythrocyte cholinesterase inhibition	A MOE of 100 is adequate for occupational exposure risk assessments. **There are no uses which result in residential exposures.**

a = The use of 100% (default) dermal absorption is required for route to route extrapolation since an oral NOAEL was selected.
b = The use of 100% (default) inhalation absorption is required for route to route extrapolation since an oral NOAEL was selected.

II. Exposure Assessment

A. Registered Uses

Two methidathion manufacturing-use products (MPs) are registered to Novartis, Inc. and Gowan Company respectively under Shaughnessy No. 100301: the 95% technical (T; EPA Reg. No. 100-530) and the 50% formulation intermediate (FI; EPA Reg. No. 10163-237). Only the Novartis 95% T and 50% FI are subject to a reregistration eligibility decision.

There are three methidathion end-use products (EPs) with food/feed uses registered to Gowan Company and Novartis, Inc.. These EPs are presented below.

EPA Reg. No.	Label Acceptance Date	Formulation Class	Product Name
10163-236 [a]	3/95	2 lb/gal EC	Supracide® 2E Insecticide-Miticide
10163-238	5/94	2 lb/gal EC	Supracide® Insecticide-Miticide
100-754[b]	5/95	25% WP	Supracide® 25 WP Insecticide-Miticide

[a] Includes CA770039, CA 820004, CA900002, FL920005, ID930003, OR930007, and WA940019.
[b] Includes ID960010, WA940020, CA970030, OR960030 and OR980021.

The following equipment is used to apply methidathion: fixed-wing aircraft, helicopter, airblast sprayer, low pressure handwand, backpack sprayer and groundboom sprayer. Methidathion is registered for use on terrestrial food crops including artichoke, citrus, clover, fruits and nuts, cotton, olives, safflowers, sun flowers, sorghum and alfalfa (grown for seed use only). Methidathion is also used on terrestrial nonfood crops like tobacco and ornamental plants. Nuts, stone fruit and citrus are the predominant use. Application rates for methidathion range from 0.25 to 10 lb ai/acre. The restricted

entry interval is 48 hours for applications of ≤2 lb ai/A or 14 days for applications at >2 lb ai/A.

The target pests include peach twig borer, scale insects, artichoke plume moth, leafminers, spider mites, boll weevil, bollworms, lygus bug, pink bollworm, whiteflies, aphids, pear psylla, mealybugs, thrips, sunflower stem weevil, sunflower moth, sunflower seed weevils, sunflower midge, Banks grass mites, flea beetles, hornworms, tobacco budworm, codling moth, and hickory shuckworms.

A comprehensive summary of the registered food/feed use patterns of methidathion, based on the product labels registered to Novartis Inc. and Gowan Company, is presented in Table A of the corresponding Residue and Product Chemistry Chapters[3]. A tabular summary of the residue chemistry science assessments for reregistration of methidathion is presented in Table B of the aforementioned chapter. The conclusions listed in Table B regarding the reregistration eligibility of methidathion food/feed uses are based on the use patterns registered by the basic producer, Novartis Corp. When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer labels.

B. Dietary Exposure

In a memorandum dated April 6, 1995[4], the HED metabolism committee determined that the residue of concern is methidathion *per se* in plants and animals. Tolerances for methidathion residues are currently expressed in terms of methidathion *per se* in plant commodities [§180.298(a and c)] and in terms of the combined residues of methidathion, its oxygen analog, and its sulfoxide and sulfone metabolites in animals [40 CFR §180.298(b)]. The qualitative nature of the residue in plants is adequately understood based on studies with [^{14}C]methidathion on cotton, tomato, artichokes, and citrus. Adequate goat and poultry metabolism studies are available. The Agency has determined that methidathion represents a 40 CFR §180.6(a)(3) situation in that there is no reasonable expectation of finite residues in animal commodities. Therefore, residues in livestock commodities are not to be regulated. This conclusion assumes cancellation of the feed uses on alfalfa, clover, and timothy and revocation of tolerances on these commodities. A summary of the methidathion tolerance reassessment and recommended modifications in commodity definitions are presented in Table C of the corresponding Residue and Product Chemistry Chapters[3].

Adequate data are available to support the established tolerances for methidathion residues in/on the commodities listed in Table C of the aforementioned Residue and Product Chemistry Chapters for this chemical[3]. The established tolerance for residues in/on citrus fruit should be increased from 2 ppm to 4 ppm, as residues of 3.4 and 3.5 ppm have been observed following registered use. The commodity definition for "Nuts" should be amended to reflect the correct crop group designation "Tree nuts," and the tolerances for pecans and walnuts, which are covered by the tree nuts group, should be deleted. The tolerance for "Peaches" is not necessary as peaches are covered by the tolerance for residues in/on "Fruits, stone;" therefore we recommend deletion of the tolerance for peaches. The group definitions "Fruits, pome" and "Fruits, stone" should be revised to "Pome fruits" and "Stone fruits," respectively.

Methidathion residue data requirements for cotton gin byproducts which result from changes in the Livestock Feeds Table (TABLE 1, OPPTS Series 860 Test Guidelines; EPA 712-C-96-169, August 1996) should be imposed at this time. However, this requirement should not impinge on the reregistration eligibility decision for methidathion. Field residue data are required on methidathion in the

plant byproducts from ginning cotton, consisting of burrs, leaves, stems, lint, and immature seeds. Cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue for the ginning process. At least three field trials for each type of harvesting (stripper and picker) are needed, for a total of six field trials. The need for additional tolerances and revisions to the exposure/risk assessments will be made upon receipt and evaluation of required data. When adequate field residue data have been submitted a tolerance must be proposed for this commodity.

The SLN label language for use on clover grown for seed contains restrictions to prevent food or feed use of treated plant parts. The feed uses on alfalfa and timothy need to be canceled, as the basic producer is not supporting these uses. But, the registrant has requested to maintain a regional registration for the use of methidathion on Kittitas County, WA. Since 85% of this crop is exported to Japan, and most of the rest is consumed by horses, the potential for dietary intake of methidathion via meat and milk consumption is negligible. However, a regional tolerance may be required for this desired use.

Any additional uses resulting in residues of methidathion in/on livestock feed items may engender the need for tolerances in/on meat, milk, poultry and eggs.

1. Acute Dietary (Food) Exposure

An acute dietary statistical exposure analysis (Monte Carlo) at the 99.9th percentile was conducted for methidathion[5]. This analysis utilized percent crop treated data obtained from a BEAD Quality Usage Assessment[6], anticipated residues and consumption data from the from the USDA Continuing Surveys of Food Intake by Individuals (CSFIIs) conducted from 1989 through 1992. This analysis for acute dietary methidathion exposure is highly refined (Tier 3), and therefore represents the best estimate of acute dietary exposure. The results of the acute analysis are presented below in Table 3.

Table 3. Acute Dietary (Food) Exposure Estimate (99.9th Percentile) and Percent of Acute RfD Occupied (Tier 3 Exposure Analysis)

Acute Dietary Risk (Food Only)		
Population	**Exposure (mg/kg/day)**	**% RfD**
U.S. Population	0.000498	25
Females (13+, nursing)	0.000442	22
Children (1-6 years)	0.001250	63
All infants < 1 yr	0.001267	63

2. Chronic Dietary (Food) Exposure

A chronic Tier 2 Dietary Residue Estimate System analysis, (DRES)[7], was conducted for methidathion incorporating percent crop treated data and some anticipated residue data. These results are summarized below in Table 4. Additional refinements could be made resulting in lower chronic dietary exposure estimates.

Table 4. Chronic Dietary (Food) Exposure Estimate and Percent of Chronic RfD Occupied (Tier 2 Exposure Analysis)

Chronic Dietary Risk (Food Only)		
Population	**Exposure (mg/kg/day)**	**% RfD**
U.S. Population	0.000137	9
Females (13+, pregnant)	0.000040	3
Children (1-6 years)	0.000338	23
Non-nursing infants <1 yr	0.000179	12

C. Dietary Drinking Water Exposure

1. Ground Water

EFED conducted Tier I, SCI-GROW (Screening Concentration in Groundwater) modeling to estimate methidathion concentrations in groundwater based on application rates of the pesticide[8]. The SCI-GROW modeling results provided HED an upper-bound Environmental Estimate Concentration (EEC) of 0.4 ppb methidathion in groundwater.

2. Surface Water

EFED conducted refined Tier II, PRIZM-EXAMS modeling to determine peak and chronic methidathion EEC's based on refined usage data and meteorological information[9]. According to EFED, based on modeling estimates, the peak and annual average concentrations of methidathion in surface waters, are 5.6 ppb and 0.6 ppb respectively.

3. Drinking Water

In addition to the modeling estimates provided above, EFED also evaluated results of available monitoring data from 264 drinking water sources from California, (259 from groundwater). This monitoring data yielded approximate averages of 4.3 ppb[9]. Based on the available information, EFED concludes that monitoring and modeling data suggest drinking water concentrations of methidathion will not exceed 6 ppb.

4. Drinking Water Levels of Comparison

Currently, HED uses drinking water levels of comparison (DWLOCs) as a surrogate to capture risk associated with exposure to pesticides in drinking water. A DWLOC is the concentration of a pesticide in drinking water that would be acceptable as an upper limit in light of total aggregate exposure to that pesticide from food, water and residential uses (if any). A DWLOC may vary with drinking water consumption patterns and body weights for specific subpopulations.

Based on the acute and chronic dietary exposure estimates presented in Tables 3 and 4, drinking water levels of comparison (DWLOCs) were calculated using the formulas listed below. A human health DWLOC is the concentration of a pesticide in drinking water which would result in unacceptable aggregate risk, after having already factored in all food exposures and other non-occupational exposures

for which OPP has reliable data.

$$DWLOC_{acute} = \frac{[\text{acute water exposure (mg/kg/day)} \times \text{(body weight)}]}{[\text{consumption (L)} \times 10^{-3}\ \text{mg}/\mu\text{g}]}$$

where acute water exposure (mg/kg/day) = aRfD - acute food exposure (mg/kg/day)

$$DWLOC_{chronic} = \frac{[\text{chronic water exposure (mg/kg/day)} \times \text{(body weight)}]}{[\text{consumption (L)} \times 10^{-3}\ \text{mg}/\mu\text{g}]}$$

where chronic water exposure (mg/kg/day) = [RfD - (chronic food exposure) (mg/kg/day)]

The Agency's default body weights and consumption values used to calculate DWLOCs are as follows: 70 kg/2L (adult male); 60kg/2L (adult females) and 10 kg/1L (child).

Since acute and chronic dietary exposures to pesticidal residues of methidathion do not exceed EPA's levels of concern, EPA used the acute and chronic RfDs and the acute and chronic exposure values to calculate the DWLOCs for the U.S. population and the two most sensitive subgroups identified in the dietary exposure assessments for acute and chronic exposures.

Acute DWLOCs

1. U.S. Population: 53 ppb

2. Children (1-6): 8 ppb

3. Females (13+, nursing): 47 ppb

By comparing the peak methidathion EECs of 6 ppb for surface water and maximum 4.3 ppb for groundwater, based on the monitoring data, to the acute DWLOCs, it is apparent that the acute DWLOCs are not exceeded for any of the population subgroups.

Chronic DWLOCs

1. U.S. Population: 48 ppb

2. Children (1-6): 12 ppb

3. Females (13+, nursing): 44 ppb

Comparing anuual avreage EECs of 0.6 ppb for surface waters and 0.4 for groundwater, it is evident that that the chronic DWLOCs are not exceeded for all of the population subgroups.

D. Occupational Exposure

Handler Exposures & Assumptions

The HIARC selected toxicological endpoints for short-term, intermediate-term, and chronic exposures[1]. The NOAEL for both short-term and intermediate-term exposure is 0.2 mg/kg/day based on a 90 day rat neurotoxicity study which focused on affects to plasma, RBC and brain ChE. Because this was based on a oral NOAEL, a 100% dermal absorption factor was used to calculate risk. A chronic exposure assessment was not required due to the absence of potential chronic exposure.

An occupational exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers during use or to persons entering treated sites after application is complete. EPA has determined that there are potential exposures to mixers, loaders, applicators, or other handlers during usual use-patterns associated with methidathion. Based on the use patterns, eight major exposure scenarios were identified for methidathion as follows.

- (1a, 1b and 1c) mixing/loading wettable powder for aerial, groundboom sprayer and airblast sprayer application;
- (2a, 2b and 2c) mixing/loading liquids for aerial, groundboom sprayer and airblast sprayer application;
- (3) liquid aerial application with a fixed-wing aircraft;
- (4) liquid groundboom sprayer application;
- (5) liquid airblast sprayer application;
- (6) liquid mixing/loading/application with a low pressure sprayer;
- (7) liquid mixing/loading/application with a backpack sprayer; and,
- (8) flagging of aerial liquid application.

These calculations of daily dose of methidathion by handlers are used to assess the risk to those handlers. For the short-term and intermediate-term risk assessments, a NOAEL of 0.2 mg/kg/day was used along with a 70 kg body weight. The short and intermediate-term dermal margins of exposure (MOEs) were less than 100 for each of the seven exposure scenarios. Generally, MOEs less than 100 exceed HED's level of concern.

Despite the potential for post-application occupational exposure, HED has decided not to assess this exposure at this time. The decision was based on the fact that all of the short-term and intermediate-term handler MOEs exceeded HED's levels of concern. Until the issues surrounding the handling of methidathion can be resolved, HED decided to postpone addressing the post application exposure.

A summary of exposure estimates and risk assessments for occupational handlers is included as Table **5**. HED's worker exposure estimates are based on surrogate data from the Pesticide Handlers Exposure Database (PHED, 8/98). Short-term and intermediate-term dermal and inhalation exposure assessments using PHED Version 1.1 surrogate data are presented in Table 5 because no chemical-specific data were submitted. Table 6 presents the corresponding risk assessment for the short-term and intermediate-term dermal and inhalation exposures including PPE and engineering controls.

There were no data for the following scenarios:

- (3) baseline and additional PPE data for aerial application of liquids with a fixed-wing aircraft. There are engineering controls data for this scenario.

- (4) baseline and additional PPE data for aerial application of liquids with a helicopter. There are engineering controls data for this scenario.

- (7) engineering controls for liquid mixing/loading/application with a low pressure handwand. There are baseline and additional PPE data for this scenario.

- (8) engineering controls for liquid mixing/loading/application with a backpack sprayer. There are baseline and additional PPE data for this scenario.

Table 5. Occupational Handler Exposure Estimate and Risk Assessment Summary							
		DERMAL			INHALATION		
		(with Minimum PPE)[a]			(No respirator)		
Mix/Loading/Appl. Scenario	**(lb ai/day)***	**UE[b] (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**	**UE[b] (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**
Mixing/Loading Exposure Scenario							
Mixing/Loading Wettable Powder for Aerial Application (1a)	1750	0.17	4.2	0.05	.043	1.1	0.18
Mixing/Loading Wettable Powder for Groundboom Application (1b)	400		0.97	0.21		0.25	0.81
Mixing/Loading Wettable Powder for Airblast Sprayer Application (1c)	200		0.5	0.40		0.12	1.6
Mixing/Loading Liquids for Aerial Application (2a)	3500	0.023	1.2	0.17	.0012	0.06	3.3
Mixing/Loading Liquids for Groundboom Application (2b)	800		0.26	0.77		0.014	14
Mixing/Loading Liquids for Airblast Sprayer Application (2c)	400		0.13	1.5		.0069	29
Applicator Exposure							
Aerial Application with a Fixed-Wing Aircraft (3)	3500	See Engineering Controls					
Groundboom (4)	800	0.015	0.17	1.2	7.0 E-4	0.0080	25
Airblast Sprayer (5)	400	0.24	1.4	0.14	.0045	0.026	7.7
Mixer/Loader/Applicator Exposure							
Low Pressure Handwand (6)	80	104	120	0.0017	.030	0.034	5.9
Backpack Sprayer (7)	80	2.5	2.9	0.069	.030	0.034	5.9
Flagger Exposure							

Table 5. Occupational Handler Exposure Estimate and Risk Assessment Summary							
		DERMAL			INHALATION		
		(with Minimum PPE)[a]			(No respirator)		
Mix/Loading/Appl. Scenario	**(lb ai/day)***	**UE[b] (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**	**UE[b] (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**
Liquid Application (8)	3500	0.010	0.50	0.40	3.5 E-4	0.018	11

*lb. ai/day = Max. Appl. Rate (lb ai/acre) * Max Area Treated (acres/day)

[a] The minimum PPE is long sleeve shirt, long pants, shoes, socks and gloves
[b]Unit Exposure (UE) is value from the Pesticide Handlers Exposure Database Ver 1.1 (PHED) Surrogate Exposure Guide (Aug 1998) and/or the Best Available Surrogate Exposure Table (BASET, 5/97)
[c]ADD(mg/kg/day) = [PHED unit exposure(mg/lb ai) * Amount handled (lb ai handled/day)] / 70 kg by wt. times 100 % absorption factor
[d]MOE = NOAEL/ADD = (0.2 mg/kg/day) / daily dermal dose.

Table 6. Occupational Handler Exposure Estimate and Risk Assessment Summary: Risk Assessment with Protective Equipment and / or Engineering Controls										
		DERMAL						INHALATION		
		(With coveralls)[a]			(With engineering controls)[b]			(With engineering controls)		
Mix/Loading/Appl. Scenario	**(lb ai/day)**	**UE[c] (mg/lb ai)**	**ADD[d] (mg/kg/day)**	**MOE[e]**	**UE (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**	**UE (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**
Mixer/Loader Exposure										
Mixing/Loading Wettable Powder for Aerial Application (1a)	1750	0.13	3.2	0.06	0.006	0.15	1.3	2.4 E-4	0.0060	33
Mixing/Loading Wettable Powder for Groundboom Application (1b)	400		0.74	0.27		0.034	5.9		0.0014	140
Mixing/Loading Wettable Powder for Airblast Sprayer Application (1c) .	200		0.37	0.54		0.017	12		6.9 E-4	290
Mixing/Loading Liquids for Aerial Application (2a)	3500	0.018	0.90	0.22	0.009	0.45	0.44	8 E-5	0.0040	50
Mixing/Loading Liquids for Groundboom Application (2b)	800		0.21	0.95		0.10	0.29		0.00091	220
Mixing/Loading Liquids for Airblast Sprayer Application (2c)	400		0.10	2.0		0.051	3.9		4.6 E-4	440
Applicator Exposure										

Table 6. Occupational Handler Exposure Estimate and Risk Assessment Summary: Risk Assessment with Protective Equipment and / or Engineering Controls										
		DERMAL						INHALATION		
		(With coveralls)[a]			(With engineering controls)[b]			(With engineering controls)		
Mix/Loading/Appl. Scenario	**(lb ai/day)**	**UE[c] (mg/lb ai)**	**ADD[d] (mg/kg/day)**	**MOE[e]**	**UE (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**	**UE (mg/lb ai)**	**ADD[c] (mg/kg/day)**	**MOE[d]**
Aerial Application with a Fixed-Wing Aircraft (3)	3500	SEE ENGINEERING CONTROLS			0.005	0.25	0.80	6.8 E-5	0.0034	59
Groundboom (4)	800	0.010	0.11	1.8	0.005	0.057	3.5	4.3 E-5	4.9 E-4	410
Airblast Sprayer (5)	400	0.22	1.3	0.15	0.14	0.80	2.5	4.0 E-4	0.0023	87
Mixer/Loader/Applicator Exposure										
Low Pressure Handwand (6)	80	6.2	7.1	0.03	NONE			NONE		
Backpack Sprayer (7)	80	1.6	1.8	0.11	NONE			NONE		
Flagger Exposure										
Liquid Application (8)	3500	0.01	0.50	0.40	0.00042	0.021	95	5.6 E-6	2.8 E-4	710

Dermal unit exposure represents long pants, long sleeve shirts, gloves, open mixing/loading, open cab tractor (open cab tractor does not apply to; 6, & 7). Baseline inhalation exposure represents no respirator.

[a] The addition of coveralls provides a 50% reduction of dermal exposure to the body (does not include head & neck)

Additional PPE dermal unit exposure represents coveralls over single layer of clothing and chemical resistant gloves, open mixing/loading, open cab tractor (open cab tractor does not apply to; 6, & 7). Unless noted otherwise, no respirators were used.

[b] Engineering controls:

Scenarios 1a, 1b and 1c: water soluble packets, double layer clothing, and gloves.

Scenarios 2a, 2b and 2c: Closed mixing/loading system, single layer clothing and gloves.

Scenarios 3: Closed cockpit, single layer clothing and no chemical resistant gloves.

Scenarios 4, and 5: Closed cab, single layer clothing and no chemical resistant gloves.

None = No engineering controls are possible.

[c] Unit Exposure (UE) is value from the Pesticide Handlers Exposure Database, Ver 1.1 (PHED) Surrogate Exposure Guide (Aug 98), and/or the Best Available Surrogate Exposure Table (BASET, 5/97)

[d]ADD(mg/kg/day) = [PHED unit exposure(mg/lb ai) * Amount handled (mg ai handled/day)] / 70 kg by wt. times 100 % absorption factor
[e]MOE = NOAEL/ADD = (0.2 mg/kg/day) / daily dermal dose.

E. Residential Exposure

There are no registered uses of methidathion that could result in residential exposures at the present time.

III. Aggregate Risk Estimates and Risk Characterization

For acute and chronic dietary risk assessments, an Uncertainty Factor (UF) of 100 was applied to account for inter-species and intra-species variability. The FQPA Safety Factor for the protection of infants and children was reduced to 1x . The acute and chronic reference doses (acute RfD and Chronic RfD) were derived by dividing the NOAEL by the UF of 100.

A. Aggregate Acute Risk Estimates

The acute dietary (food) risk estimates for methidathion do not exceed HED's level of concern. EFED modeling estimates from (SCI-GROW) for groundwater; and PRIZM/EXAMS modeling estimates as well as monitoring results for surface waters; do not exceed the DWLOC for acute aggregate exposure.

The highly refined statistical acute dietary (food) exposure analysis was conducted for methidathion using percent crop treated data and anticipated residues at the 99.9th percentile. Thus, this analysis for methidathion acute dietary exposure represents a best estimate (Tier 3).

B. Short and Intermediate-Term Aggregate Risk Estimate

Because methidathion does not have any registered uses that could result in residential exposures, aggregate short and intermediate-term risk assessments are not required.

C. Chronic Aggregate Risk Estimate

The chronic dietary (food) risk estimates for methidathion do not exceed HED's level of concern. EFED modeling estimates (SCI-GROW) for levels of methidathion in ground water, as well as modeling estimates (PRIZM/EXAMS) and monitoring results do not exceed the DWLOC for chronic aggregate exposure.

The chronic dietary (food) risk assessment, was partially refined using some percent crop treated data and some anticipated residues. Further use of anticipated residues and/or percent of crop treated, as well as monitoring data would further reduce chronic dietary (food) exposure and risk estimates.

D. Occupational

Risk Estimates From Handler Exposures

Short-Term and Intermediate-Term Risk

The calculations of risk indicate that the margins of exposure (MOEs) are less than 100 at **baseline** *(note: this baseline includes single layer, gloves, open mixing/loading, and open cab)* for short-term and intermediate-term risk for all mixer/loader and applicator scenarios. The addition of personal protective equipment (PPE) and engineering controls still do not raise the MOEs above the HED criterion of MOE 100.

The calculations of risk indicate that the MOEs are less than 100 despite maximum mitigation

measures for all eight mixer/loader and applicator scenarios; ***except for the following inhalation scenarios: 1b, 1c, 2b, 2c, 4, and 8.***

Risk Estimates From Post-Application Exposures

Despite the potential for post-application exposure, EPA/HED has decided not to assess this exposure at this time. The decision was based on the fact that all of the short-term and intermediate-term dermal MOEs were unacceptable. Until the issues surrounding the handling of methidathion can be resolved, EPA/HED has postponed assessing the post application exposure.

V. Data Needs

Field Crop Trial data on cotton gin-byproducts. (OPPTS Series 860 Test Guidelines)

VI. References

1. Rowland, J., Methidathion - Report of the Hazard Identification Assessment review Committee.

October 8, 1997.

2. Tarplee, B. And Rowland, J., FQPA Safety Factor Recommendations for the Organophosphates. August 6, 1998.

3. Smith, W.O., Methidathion. Product and Residue Chemistry Chapters for the Reregistration Eligibility Decision Document (RED). June 11, 1996.

Smith, W.O., Methidathion. Addendum to Residue Chemistry Chapter of RED. November 21, 1996.

Smith, W.O., Methidathion Follow-up to Residue Chemistry Chapter of the RED. December 3, 1996.

4. Perfetti, R., Report of the HED Metabolism Committee Held on April 4, 1995: Methidathion. April 6, 1995.

5. Smith, W.O., Methidathion. Acute Dietary Risk Assessment (Monte Carlo Analysis). October 16, 1998.

6. Grube, A., BEAD Qualitative Usage Analysis Table for Methidathion. February, 20, 1996.

7. Steinwand, B., Dietary Exposure Analysis for Methidathion in Support of the Reregistration Eligibility Decision. January 8, 1997.

8. Lin, J., Tier 1: Screen for Drinking Water Assessment of Methidathion. December 17, 1997.

9. Lin, J., Methidathion - Tier 3 Drinking Water Assessment. December 30, 1998.